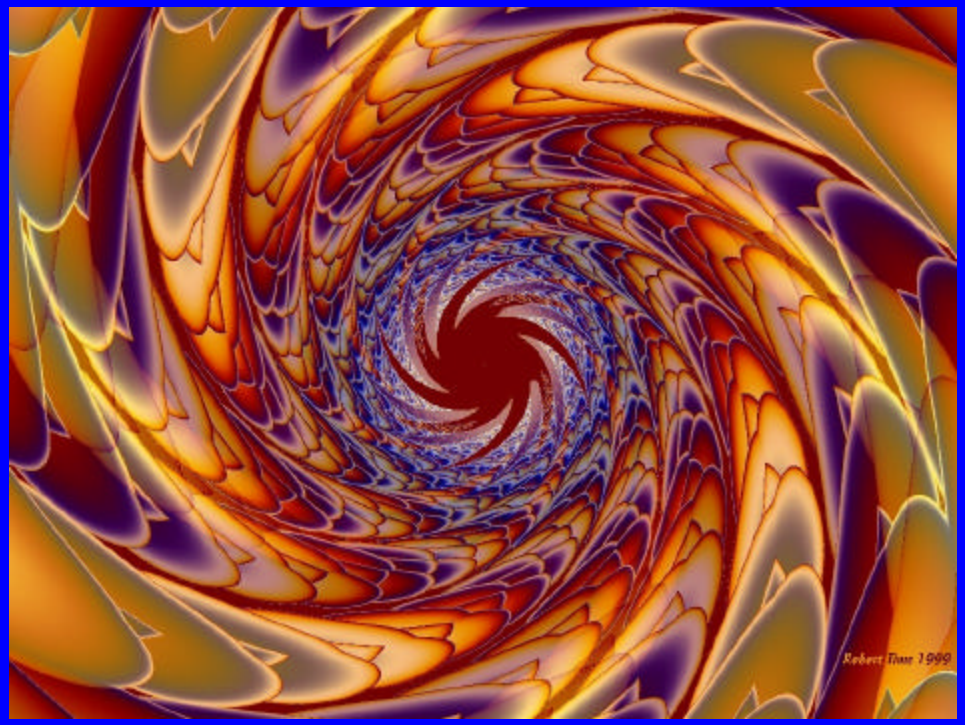
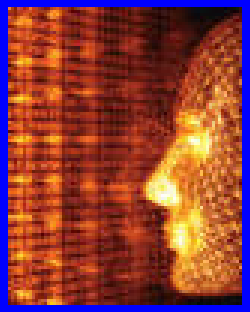
CBER 2004 Update: Innovation Advancing Public Health



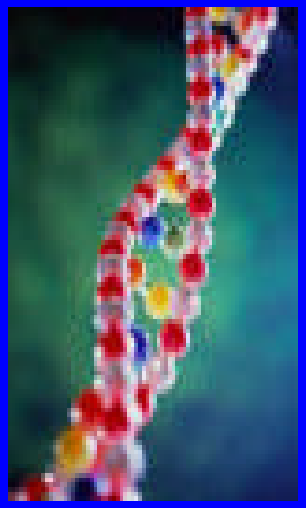
Karen Midthun, M.D.
Deputy Director, Medical
Center for Biologics and Research (CBER)
RAPS October, 2004

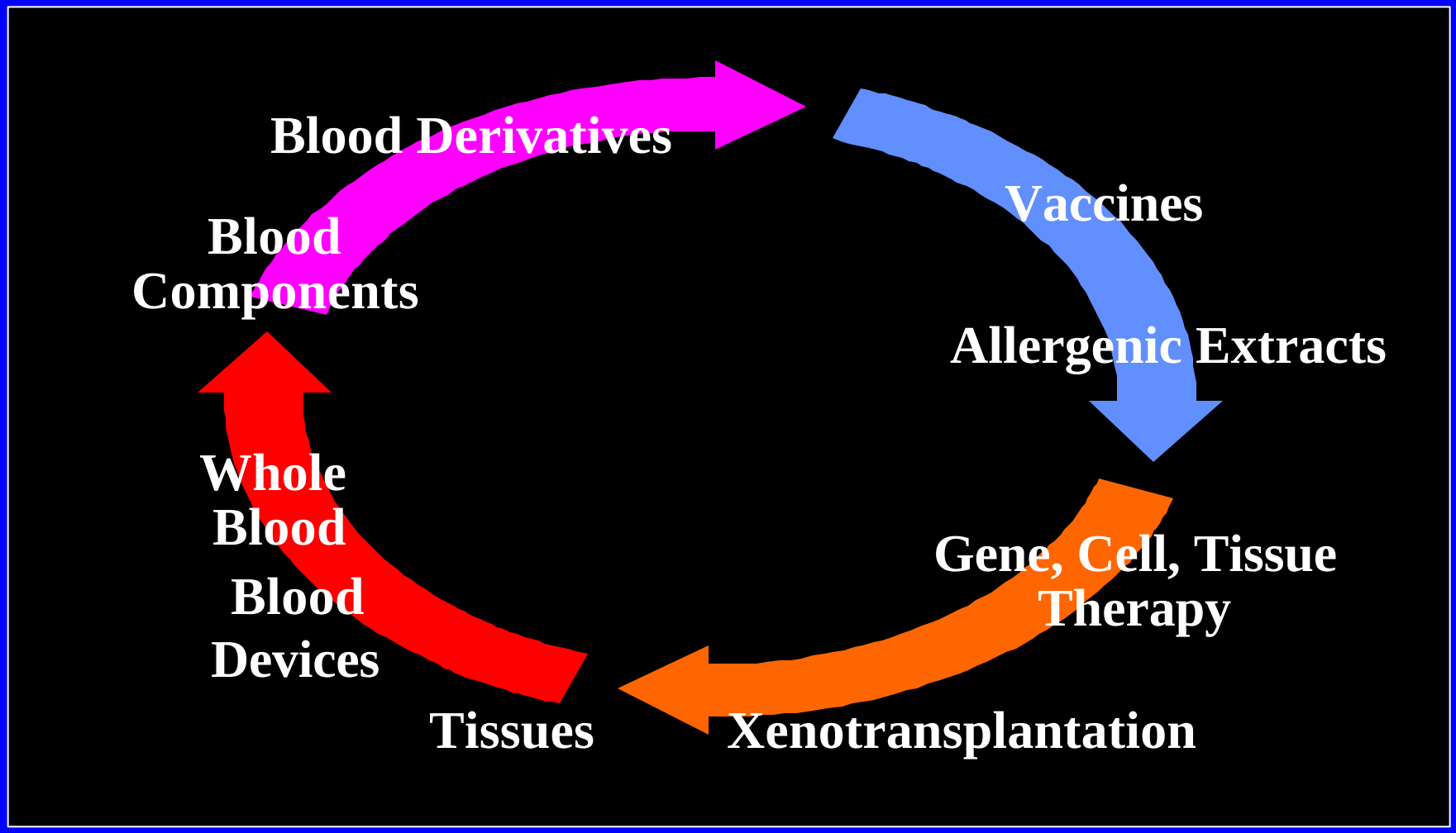


Vision for CBER

INNOVATIVE TECHNOLOGY ADVANCING PUBLIC HEALTH

- ***Protect and improve public and individual health in the US and, where feasible, globally***
- ***Facilitate the development, approval and access to safe and effective products and promising new technologies***
- ***Strengthen CBER as a preeminent regulatory organization for biologics***




Blood Derivatives
Vaccines
Blood Components
Allergenic Extracts
Whole Blood
Gene, Cell, Tissue Therapy
Blood Devices
Tissues
Xenotransplantation

Presentation Summary

- Selected CBER Accomplishments
- CBER 2004: Major Initiatives
- CBER – Fostering Innovation
- CBER Science & Critical Path

Selected Accomplishments

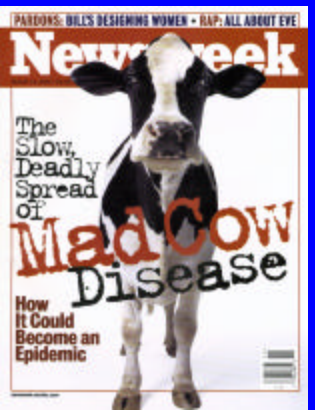
- **FDA's GMPs for 21st Century Initiative**
  - **Major role on Steering Committee and subcommittees**
  - **CBER already had adopted many "new" practices endorsed by FDA, e.g.,**
    - **Scientists on inspections, specialized teams/training, risk based prioritization, Center review of warning letters**
    - **New CBER system-based, risk-based compliance programs for inspections/ enforcement have been developed or are nearing completion**

Selected Accomplishments

- **Public Health**
  - **Pandemic flu:**
    - **Key role in HHS' 8/26/2004 preparedness plan**
    - **Assisting in landmark effort to produce H5N1 vaccine (manufacturing reagents, etc)**
  - **WNV Blood Donor Screening Test in 8 months – Secretary's Award**
  - **Successful response to blood "white particles," SARS, and other Emerging Infectious Disease events - outreach on product development, e.g., with CDC/NIH in assuring provision of suitable isolates of SARS coronavirus; testing viral inactivation methods and parameters**

Selected Accomplishments

- **Public Health-**
  - **Continued phase in of thimerosol free/reduced vaccines**
  - **New HIV, Hepatitis C tests, TRANSNET Monitoring Pilot**
  - **Other new products, e.g. tD, Flumist vaccine, fibrin sealant, a-1 proteinase, OraQuik**
- **Risk Assessment/Guidances re: TSE, CT, blood safety**



Selected Accomplishments

- **Counterterrorism**
  - **Now ~ 25% of CBER effort/resources**
  - **Proactive needs/gap assessments/inventories**
  - **Emergency availability of critical countermeasures for smallpox, botulinum and anthrax (vaccines/blood/ immunoglobulins)**
  - **Critical participation in multiple Task Forces re: Product Development including industry, CDC, NIH and DOD**
  - **Proactive site visits/manufacturers' assistance**
  - **Implement Project BioShield**

Selected Accomplishments

- Patient Safety
  - **Joint CBER/CDER risk, pharmacovigilence and data monitoring committee guidances**
  - **Collaborate w/CMS and UHC on vaccine/tissue safety**
  - **VAERS data-mining projects**
- **New Technologies**
  - **Gene therapy long-term follow-up meeting**
  - **Cancer vaccines into Phase III**
  - **BRMACs on islet cells & cell Rx for cardiac disease**
  - **Cellular product CMC review guidance, vaccine cell substrate guidance**
  - **Work on microarray standards, xeno safety, stem cell characterization, CT products**

Selected Accomplishments

- **International Efforts**
  - **Re-designated WHO Collaborating Center**
  - **New MOUs: EU, Canada, Switzerland**
  - **ICH (including GT), PICS, ICDRA**
  - **Xeno,Tissue and Gene Rx outreach with WHO, others**
  - **Plasma derivative, thrombin outreach and standards**

Selected Accomplishments

- **IT**
  - **CBER Agency Leader in e-submissions and secure digitally signed correspondence (e-labeling, barcode, EDR & VAERS enhancements)**
  - **2003 Secretary's Award in e-government**
  - **GEMCRIS: Secretary's Award (with NIH)**
  - **Under consolidated IT, Agency Lead for Gateway**

Selected Accomplishments

- **Communications and Outreach:**
  - HIV vaccine meetings; Workshops on CT Product Development; Anthrax therapeutics (joint w/ CDER); plasma standards; Bayesian and adaptive trial designs
  - Initiation of manufacturing site visit program
  - 2 million Web hits/month, 3 listservs
  - Rapid Dissemination of Critical Data, e.g.,
    - **Outstanding responses to counterfeiting: e.g. Epogen/Procrit**
    - **Biologic Storage in Preparation for recent hurricanes**

CBER 2004: Major Initiatives

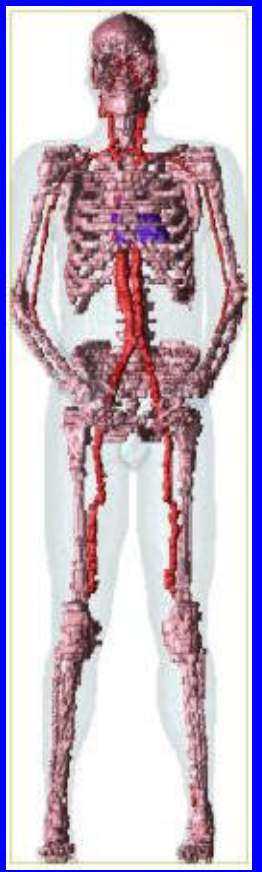
- **Efficient Risk Management**
  - **Enhanced Review Management and Processes**
    - **Review Template Initiative: to enhance consistency & quality of review and submissions; facilitate electronic processes**
      - **Clinical, pharm/tox, CMC, statistical**
    - **Identify best practices/management and prepare for Agency-wide quality initiatives**

CBER 2004: Major Initiatives

- GMPs for 21st Century Initiative
- Continued PDUFA/MDUFMA timeframe adherence
- Review Management Updates
  - **Monthly town hall meetings for all CBER staff, especially reviewers**
  - **Topics suggested by staff, with Qs & As at each presentation**

CBER 2004: Major Initiatives

- Patient Safety -Tissue Safety System
  - Final Donor Suitability & Good Tissue Practice Rules
  - Developing new CBER-CDRH Tissue Engineering Review Program (single portal of entry)
  - Creation of interdisciplinary Tissue Safety Team -
    - Active Surveillance as a goal
    - – Adverse Event Reports and Analysis
    - – Training, outreach, inspection and compliance



CBER 2004: Major Initiatives

- Counterterrorism
  - CT Coordinating Committee
  - Bioshield related guidance and evaluation
  - Spore former guidance
  - EUA law and draft guidance, new approach to product labeling for strategic stockpile
  - CT Product Safety Planning
    - **AVA “final rule”; Baby BIG approval, VIG availability**
    - **Progress in SPx and anthrax vaccines**
    - **Measures to reduce potential vulnerabilities of CBER products essential to response to terrorist events**

CBER 2004: Major Initiatives

- **Global Vaccine Assistance**
  - March 2004 PAHO meeting – opportunities for increased training and technical consultation
  - Increasing focus on harmonization, e.g., w/ EMEA; encourage global vaccine development plans

CBER: Approaches to Fostering Innovation

- Innovation through leadership & management
  - positive culture
  - problem solving, teamwork, partnerships
  - learning from successes and failures
  - efficiently used human and material resources
  - result-remove barriers, build bridges, improve efficiency
  - Develop succession and mentorship plans to enhance leadership at all levels

CBER: Approaches to Fostering Innovation

- Innovation in review and science
  - expert & science-based approaches to all processes e.g. review, risk management & communication
  - focus on helping new fields coalesce & move forward
    - Provide guidance and clarity
    - Identify problems; help bring about and make available needed solutions and tools e.g. “Critical Path”

CBER Science & Critical Path Initiative

- **CBER Initiatives to Track and Focus Research Consistent with and Supportive of FDA Initiative**
- **Target unmet needs with regulatory implications to facilitate development of products**
- **Seek increased outside participation/input**
  - Collaborations with multiple outside institutions
  - Plan to extend AC evaluation to broad programmatic areas & include identifying unmet needs and opportunities

CBER Science & Critical Path Initiative

- Benefits multiple sponsors; high impact for new fields, products w/ uncertain markets, public health
- Maintains staff “cutting edge” expertise needed for dealing with evolving biotechnologies
  - Scientific expertise and confidence foster objectivity
    - Reduces risks of reflexive over- or under-protectiveness
    - Make regulation more scientific, less “defensive”

Examples of Critical Path Opportunities

- New vaccine delivery systems/methods, rapid use vectors, adjuvants
- Develop/make available well-characterized cell banks (and assays for safety/adventitious agents) useful for vaccine and other biologic production – and update guidance for use
- Characterize cell therapies & link to standardized clinical/lab outcomes, e.g. HPSCs
- Methods & validation of pathogen inactivation for blood, plasma, tissues and other products
- Multipathogen and rapid detection methods for biologics including blood and tissue products
- Improve longevity/storage of blood and tissues

Thanks!

- ***We're proud of our staff & mission. CBER sees a bright, promising future.***
- ***Together, we can continue to enhance development of safe and effective products that promote public health.***
- ***We seek your input and want to work with you and know about your needs, strategies and ideas.***

CBER: INNOVATIVE TECHNOLOGY ADVANCING PUBLIC HEALTH

CBER PDUFA II Application Review Performance

Cohort Years FY 1998 – FY 2002

Performance Goals		PDUFA II									
		FY 1998		FY 1999		FY 2000		FY 2001		FY 2002*	
		Performance	Goal	Performance	Goal	Performance	Goal	Performance	Goal	Performance	Goal
BLAs	Standard: 10 months			**100%**	30%	**100%**	50%	**100%**	70%	**100%**	90%
	12 months	**100%**	90%	**100%**	90%	**100%**	90%	**100%**	90%		
	Priority: 6 months	**100%**	90%	**100%**	90%	**100%**	90%	**100%**	90%	**100%**	90%
Efficacy Supplements	Standard: 10 months			**100%**	30%	**100%**	50%	**100%**	70%	**83%**	90%
	12 months	**100%**	90%	**100%**	90%	**100%**	90%	**100%**	90%		
	Priority: 6 months	**100%**	90%	**100%**	90%	**100%**	90%	**100%**	90%	**100%**	90%
Manufacturing Supplements	Prior Approval: 4 months			**92%**	30%	**92%**	50%	**95%**	70%	**99%**	90%
	6 months	**99%**	90%	**100%**	90%	**94%**	90%	**96%**	90%		
	CBE and CBE-30: 6 months	**99%**	90%	**96%**	90%	**97%**	90%	**94%**	90%	**99%**	90%
Resubmissions	Class 1: 2 months	**100%**	30%	**100%**	50%	**100%**	70%	**100%**	90%	**100%**	90%
	4 months	**100%**	90%	**100%**	90%	**100%**	90%	**100%**	90%		
	Class 2: 6 months	**100%**	90%	**100%**	90%	**100%**	90%	**100%**	90%	**100%**	90%

*Performance percentages do not include submissions transferred to CDER that were pending on October 1, 2003.

CBER PDUFA II Procedural Goals Performance

Cohort Years FY 1998 – FY 2002

Performance Goals	FY 1998		FY 1999		FY 2000		FY 2001		FY 2002	
	Performance	Goal	Performance	Goal	Performance	Goal	Performance	Goal	Performance	Goal
Meeting Management										
Respond to Meeting Request: 14 days			**73%**	70%	**97%**	80%	**98%**	90%	**98%**	90%
Meeting Held: 30, 60, 75 days			**88%**	70%	**94%**	80%	**97%**	90%	**98%**	90%
Minutes Finalized: 30 days			**86%**	70%	**91%**	80%	**97%**	90%	**96%**	90%
Special Protocol Question Requests										
Assessment: 45 days			**--**	60%	**--**	70%	**100%**	80%	**100%**	90%
Major Dispute Resolution										
Respond to Request: 30 days			**100%**	70%	**--**	80%	**100%**	90%	**100%**	90%
Clinical Holds										
Respond to Complete Response: 30 days	**82%**	75%	**95%**	90%	**98%**	90%	**92%**	90%	**98%**	90%

"--" means no requests were received.

CBER PDUFA III Application Review Performance

Cohort Years FY 2003 – FY 2007

Performance Goals		PDUFA III									
		FY 2003		FY 2004*		FY 2005		FY 2006		FY 2007	
		Performance	Goal	Performance	Goal	Performance	Goal	Performance	Goal	Performance	Goal
BLAs	Standard: 10 months	**100%**	90%	**100%**	90%	--	90%	--	90%	--	90%
	Priority: 6 months	**100%**	90%	--	90%	--	90%	--	90%	--	90%
Efficacy Supplements	Standard: 10 months	**100%**	90%	--	90%	--	90%	--	90%	--	90%
	Priority: 6 months	**100%**	90%	--	90%	--	90%	--	90%	--	90%
Manufacturing Supplements	Prior Approval: 4 months	**99%**	90%	**100%**	90%	--	90%	--	90%	--	90%
	CBE and CBE-30: 6 months	**99%**	90%	**100%**	90%	--	90%	--	90%	--	90%
BLA Resubmissions	Class 1: 2 months	**100%**	90%	--	90%	--	90%	--	90%	--	90%
	Class 2: 6 months	**100%**	90%	--	90%	--	90%	--	90%	--	90%
Efficacy Supplement Resubmissions	Class 1: 2 months	**100%**	30%	--	50%	--	70%	--	80%	--	90%
	Class 1: 4 months			--	90%	--	90%	--	90%		
	Class 1: 6 months	**100%**	90%								
	Class 2: 6 months	**100%**	90%	--	90%	--	90%	--	90%	--	90%
Review Notifications	1st Cycle: 74 days	**100%**	50%	**100%**	70%	--	90%	--	90%	--	90%

Percentages are for requests for which the goal date has been reached; Dashes (--) indicate no submissions of this type or the goal date has not been reached for any of the submissions; Percentages for FY 2003 do not include OTRR/ODEVI requests pending as of October 1, 2003

*Data through 6/30/04

CBER PDUFA III Procedural Goals Performance

Cohort Years FY 2003 – FY 2007

Performance Goals	FY 2003		FY 2004		FY 2005		FY 2006		FY 2007	
	Performance	Goal	Performance	Goal	Performance	Goal	Performance	Goal	Performance	Goal
Meeting Management										
Respond to Meeting Request: 14 days	**98%**	90%	**97%**	90%	--	90%	--	90%	--	90%
Meeting Held: 30, 60, 75 days	**99%**	90%	**99%**	90%	--	90%	--	90%	--	90%
Minutes Finalized: 30 days	**98%**	90%	**96%**	90%	--	90%	--	90%	--	90%
Special Protocol Question Requests										
Assessment: 45 days	**100%**	90%	**100%**	90%	--	90%		90%	--	90%
Major Dispute Resolution										
Respond to Request: 30 days	--	90%	–	90%	--	90%		90%	--	90%
Clinical Holds										
Respond to Complete Response: 30 days	**97%**	90%	**98%**	90%	--	90%		90%	--	90%

Percentages are for requests for which the goal date has been reached; Dashes (--) indicate no submissions of this type or the goal date has not been reached for any of the submissions; Percentages for FY 2003 do not include OTRR/ODEVI requests pending as of October 1, 2003

*Data through 8/31/04

(L-262)RIMS:9/16/04

CBER Review Performance

FY 2003 Cohort of User Fee Applications*

Application Types	Numbers				Percent of Actions	
	Submitted	Filed	AP	RTF, UN, or WF	Within Goal	Overdue
New Products	8	8	2	0	100%	0%
Effectiveness Supplements	16	15	4	1	100%	0%
Manufacturing Supplements	903	897	656	6	99%	1%

Submissions pending action as of October 1, 2003 and transferred to CDER are included in CBER receipts but not final actions or percentages Within Goal/Overdue.

AP=Approved, RTF=Refuse To file, UN=Unacceptable For Filing, WF=Withdrawn Before Filing

Data through 6/30/04

(L-259)RIMS:08/25/04

CBER Review Performance

FY 2004* Cohort of User Fee Applications

Application Types	Numbers				Percent of Actions	
	Submitted	Filed	AP	RTF, UN, or WF	Within Goal	Overdue
New Products	3	3	0	0	33%	0%
Effectiveness Supplements	6	6	0	0	--%	--%
Manufacturing Supplements	478	475	200	3	41%	0%

AP=Approved, RTF=Refuse To file, UN=Unacceptable For Filing, WF=Withdrawn Before Filing

*Data as of 6/30/04

(L-260)RIMS:08/25/04

CBER Device Application Receipts

FY 2002 – FY 2004*

		MDUFMA	
	FY02	FY03	FY04*
PMAs (Traditional)	0	0	0
PMAs (Modular)	1	3	1
PMSs (180 Day)	5	3	3
510(k)s (All Types)	40	65	75
BLAs (Original)	2	0	8
BLSs (Efficacy)	0	3	0
BLSs (Manuf, PAS)	35	75	85

*FY 2004 data through August 31, 2004

CBER 510k Review Time Performance

Receipt to Final Action
FY 2002-FY 2004*

		MDUFMA	
	FY02	FY03	FY04*
CBER Review Time (days)	119.1	58.2	59.0
Average Number of Cycles	1.7	1.3	1.3

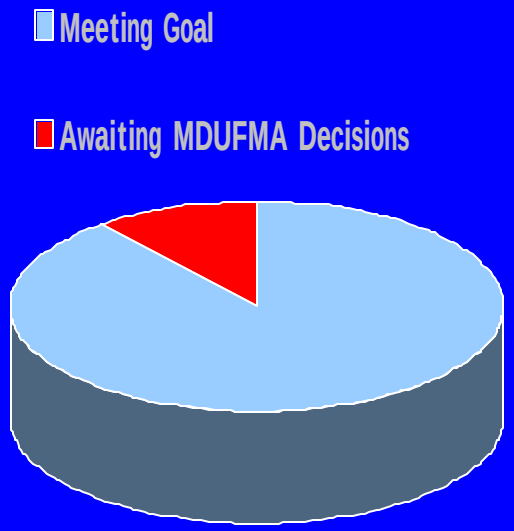
Includes SEs/NSEs/WDs

*FY 2004 data through August 31, 2004

MDUFMA Performance
510(k) Applications

Goal: Decision within 90 total FDA days

	1st QTR FY 03	2nd QTR FY 03	3rd QTR FY 03	4th QTR FY 03	Annual Totals FY 03
Total Received	20	14	12	19	65
Total Filed	20	14	12	19	65
Meeting Goal	20	14	12	12	58 (89%)
Not Meeting Goal	0	0	0	0	0
Awaiting MDUFMA Decision	0	0	0	7	7 (11%)



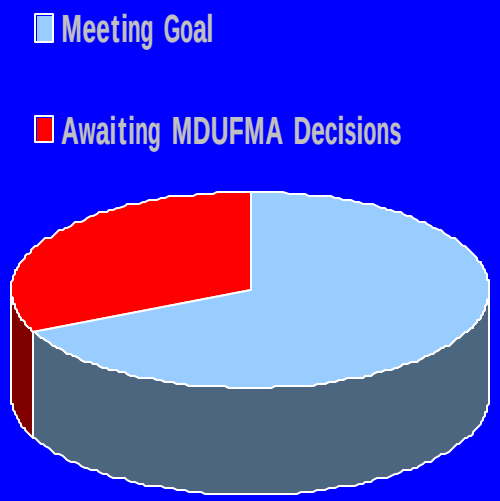
FY 2003 Cohort

(as of 8/31/04)

MDUFMA Performance
510(k) Applications

Goal: Decision within 90 total FDA days

	1st QTR FY 04	2nd QTR FY 04	3rd QTR FY 04	4th QTR FY 04	Annual Totals FY 04
Total Received	18	21	26	10	75
Total Filed	18	21	26	10	75
Meeting Goal	18	17	16	0	51 (68%)
Not Meeting Goal	0	0	0	0	0
Awaiting MDUFMA Decision	0	4	10	10	24 (32%)



FY 2004 Cohort

(as of 8/31/04)